

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 5, line 12 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Non-metabolic actions of amylin include vasodilator effects which may be mediated by interaction with CGRP vascular receptors. Reported *in vivo* tests suggest that amylin is at least about 100 to 1000 times less potent than CGRP as a vasodilator (*Brain et al., Eur. J. Pharmacol.*, 183:2221 (1990); *Wang et al., FEBS Letts.*, 291:195-198 (1991)). The effect of amylin on regional hemodynamic actions, including renal blood flow, in conscious rats has been reported (*Gardiner et al., Diabetes*, 40:948-951 (1991)). The authors noted that infusion of rat amylin was associated with greater renal vasodilation and less mesenteric vasoconstriction than is seen with infusion of human α -CGRP. They concluded that, by promoting renal hyperemia to a greater extent than did α -CGRP, rat amylin could cause less marked stimulation of the renin-angiotensin system, and thus, less secondary angiotensin II-mediated vasoconstriction. It was also noted, however, that during coinfusion of human α -⁸⁻³⁷CGRP [SEQIDNO:16] (SEQ ID NO:16) and rat amylin, renal and mesenteric vasoconstrictions were unmasked, presumably due to unopposed vasoconstrictor effects of angiotensin II, and that this finding is similar to that seen during coinfusion of human α -CGRP and human α -⁸⁻³⁷CGRP [SEQIDNO:16] (SEQ ID NO:16) (*id.* at 951).

Please replace the paragraph beginning at page 6, line 27 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Injected into the brain, or administered peripherally, amylin has been reported to suppress food intake, *e.g.*, *Chance et al., Brain Res.*, 539:352-354 (1991) and *Chance et al., Brain Res.*, 607:185-188 (1993), an action shared with CGRP and calcitonin. The effective concentrations at the cells that mediate this action are not known. Since the work described by the inventors

herein with regard to the effect of amylin and amylin agonists to decrease body weight in humans, several publications have reported that infusion of amylin can cause anorexia in rats. See Arnelo *et al.*, *Am. J. Physiol.*, 40:R1654-R1659 (1996); Arnelo *et al.*, *Scan. J. Gastroenterol.*, 31:83-89 (1996) (1996).

Please replace the paragraph beginning at page 9, line 2 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

We have now discovered, surprisingly, that amylin, as well as amylin agonists, for example, the amylin agonist analogue ^{25,28,29}Pro-h-amylin ~~[SEQ. ID. NO. 1]~~ (SEQ ID NO:1) (also referred to as "pramlintide" and previously referred to as "AC-0137"), can be used for treatment of obesity in humans.

Please replace the paragraph at page 10, lines 6-7 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Further, amylin agonist analogues useful in the methods of this application include amylin agonist analogues having the following amino acid sequence ~~[SEQ ID NO:23]~~ (SEQ ID NO:23):

Please replace the paragraph beginning at page 13, line 11 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

In a preferred embodiment, the amylin agonist is an amylin agonist analogue, preferably, ^{25, 28, 29}Pro-h-amylin ~~[SEQ ID NO:1]~~ (SEQ ID NO:1).

Please replace the paragraph at page 13, line 23 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

1. An agonist analogue of amylin having the amino acid sequence [SEQ ID NO:17] **(SEQ ID NO:17):**

Please replace the paragraph at page 14, line 20 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

2. An agonist analogue of amylin having the amino acid sequence [SEQ ID NO:18] **(SEQ ID NO:18):**

Please replace the paragraph at page 15, line 20 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

3. An agonist analogue of amylin having the amino acid sequence [SEQ ID NO:19] **(SEQ ID NO:19):**

Please replace the paragraph at page 16, line 16 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

4. An agonist analogue of amylin having the amino acid sequence [SEQ ID NO:20] **(SEQ ID NO:20):**

Please replace the paragraph beginning at page 17, line 11 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preferred amylin agonist analogues include ^{25,28,29}Pro-h-amylin [SEQ ID NO:1] (SEQ ID NO:1), ¹⁸Arg^{25,28,29}Pro-h-amylin [SEQ ID NO:2] (SEQ ID NO:2) and ¹⁸Arg^{25,28}Pro-h-amylin [SEQ ID NO:3] (SEQ ID NO:3).

Please replace the paragraph beginning at page 25, line 18 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of ^{25,28,29}Pro-h-Amylin [SEQ ID NO:1] (SEQ ID NO:1)

Solid phase synthesis of ^{25,28,29}Pro-h-amylin [SEQ ID NO:1] (SEQ ID NO:1) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ^{25,28,29}Pro-h-amylin [SEQ ID NO:1] (SEQ ID NO:1) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3,949.

Please replace the paragraph beginning at page 26, line 2 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of ¹⁸Arg^{25,28,29}Pro-h-Amylin [SEQ ID NO:2] (SEQ ID NO:2)

Solid phase synthesis of ¹⁸Arg^{25,28,29}Pro-h-amylin [SEQ ID NO:2] (SEQ ID NO:2) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with

thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{18}\text{Arg}^{25,28,29}\text{Pro-h-amylin }$ [SEQ ID NO:2] (SEQ ID NO:2) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(\text{M}+\text{H})^+=3,971$.

Please replace the paragraph beginning at page 26, line 15 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of $^{18}\text{Arg}^{25,28}\text{Pro-h-Amylin }$ [SEQ ID NO:3] (SEQ ID NO:3)

Solid phase synthesis of $^{18}\text{Arg}^{25,28}\text{Pro-h-amylin }$ [SEQ ID NO:3] (SEQ ID NO:3) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The $^{2,7}\text{-[disulfide]amylin-MBHA-resin}$ was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{18}\text{Arg}^{25,28}\text{Pro-h-amylin }$ [SEQ ID NO:3] (SEQ ID NO:3) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(\text{M}+\text{H})^+=3,959$.

Please replace the paragraph beginning at page 27, line 3 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Evaluation of the binding of compounds to amylin receptors was carried out as follows.
 ^{125}I -rat amylin [SEQ ID NO:21] (SEQ ID NO:21) (Bolton-Hunter labeled at the N-terminal

lysine) was purchased from Amersham Corporation (Arlington Heights, IL). Specific activities at time of use ranged from 1950 to 2000 Ci/mmol. Unlabeled peptides were obtained from BACHEM Inc. (Torrance, CA) and Peninsula Laboratories (Belmont, CA).

Please replace the paragraph beginning at page 27, line 18 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

To measure ^{125}I -amylin [SEQ ID NO:22] (SEQ ID NO:22) binding, membranes from 4 mg original wet weight of tissue were incubated with ^{125}I -amylin [SEQ ID NO:22] (SEQ ID NO:22) at 12-16 pM in 20 mM HEPES buffer containing 0.5 mg/ml bacitracin, 0.5 mg/ml bovine serum albumin, and 0.2 mM PMSF. Solutions were incubated for 60 minutes at 23°C. Incubations were terminated by filtration through GF/B glass fiber filters (Whatman Inc., Clifton, NJ) which had been presoaked for 4 hours in 0.3% polyethyleneimine in order to reduce nonspecific binding of radiolabeled peptides. Filters were washed immediately before filtration with 5 ml cold PBS, and immediately after filtration with 15 ml cold PBS. Filters were removed and radioactivity assessed in a gamma-counter at a counting efficiency of 77%. Competition curves were generated by measuring binding in the presence of 10^{-12} to 10^{-6} M unlabeled test compound and were analyzed by nonlinear regression using a 4-parameter logistic equation (INPLOT program; GRAPHPAD Software, San Diego).

Please replace Table II beginning at page 30, line 1 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

TABLE II

Receptor Binding	Soleus Muscle
<u>Assay IC₅₀(pM)</u>	<u>Assay EC₅₀(nM)</u>

1)	^{28}Pro -h-Amylin	15.0	2.64
[SEQ. ID. NO. 4] (SEQ ID NO:4)			
2)	$^{25}\text{Pro}^{26}\text{Val}^{28,29}\text{Pro}$ -h-Amylin	18.0	4.68
[SEQ. ID. NO. 5] (SEQ ID NO:5)			
3)	$^{2,7}\text{Cyclo-}[^2\text{Asp},^7\text{Lys}]\text{-h-Amylin}$	310.0	6.62
[SEQ. ID. NO. 6] (SEQ ID NO:6)			
4)	$^{2-37}\text{h-Amylin}$	236.0	1.63
[SEQ. ID. NO. 7] (SEQ ID NO:7)			
5)	^1Ala -h-Amylin	148.0	12.78
[SEQ. ID. NO. 8] (SEQ ID NO:8)			
6)	^1Ser -h-Amylin	33.0	8.70
[SEQ. ID. NO. 9] (SEQ ID NO:9)			
7)	^{29}Pro -h-Amylin	64.0	3.75
[SEQ. ID. NO. 10] (SEQ ID NO:10)			
8)	$^{25,28}\text{Pro}$ -h-Amylin	26.0	13.20
[SEQ. ID. NO. 11] (SEQ ID NO:11)			
9)	des- $^1\text{Lys}^{25,28}\text{Pro}$ -h-Amylin	85.0	7.70
[SEQ. ID. NO. 12] (SEQ ID NO:12)			
10)	$^{18}\text{Arg}^{25,28}\text{Pro}$ -h-Amylin	32.0	2.83
[SEQ. ID. NO. 3] (SEQ ID NO:3)			
11)	des- $^1\text{Lys}^{18}\text{Arg}^{25,28}\text{Pro}$ -h-Amylin	82.0	3.77
[SEQ. ID. NO. 13] (SEQ ID NO:13)			
12)	$^{18}\text{Arg}^{25,28,29}\text{Pro}$ -h-Amylin	21.0	1.25

[SEQ ID NO:2] (SEQ ID NO:2)

13) des-¹Lys¹⁸Arg^{25,28,29}Pro-h-Amylin 21.0 1.86

[SEQ ID NO:14] (SEQ ID NO:14)

14) ^{25,28,29}Pro-h-Amylin 10.0 3.71

[SEQ ID NO:1] (SEQ ID NO:1)

15) des-¹Lys^{25,28,29}Pro-h-Amylin 14.0 4.15

[SEQ ID NO:15] (SEQ ID NO:15)

Please replace the paragraph beginning at page 33, line 2 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of ²⁸Pro-human-Amylin [SEQ ID NO:4] (SEQ ID NO:4)

Solid phase synthesis of this analogue of human ("h-") amylin using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin- MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid hydrofluoric acid ("HF") in the presence of dimethylsulfide and anisole. The ²⁸Pro-h-amylin [SEQ ID NO:4] (SEQ ID NO:4) was purified by preparative HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+1)/e=3914.

Please replace the paragraph beginning at page 33, line 16 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of $^{25}\text{Pro}^{26}\text{Val}^{28,29}\text{Pro}$ -h-Amylin [SEQ ID NO:5] (SEQ ID NO:5)

Solid phase synthesis of this amylin analogue using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The 2,7 -[disulfide]amylin-MBHA-resin was obtained by treatment with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{25}\text{Pro}^{26}\text{Val}^{28,29}\text{Pro}$ -h-amylin [SEQ ID NO:5] (SEQ ID NO:5) was purified by preparative HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+1)/e=3936.

Please replace the paragraph beginning at page 34, line 2 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of $^{2,7}\text{Cyclo-[}^2\text{Asp,}^7\text{Lys]}$ -h-Amylin [SEQ ID NO:6] (SEQ ID NO:6)

Solid phase synthesis of this amylin analogue using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. ^2Asp and ^7Lys were introduced with Boc- $^2\text{Asp(Fmoc)-OH}$ and Boc- $^7\text{Lys(Fmoc)-OH}$. Following selective side-chain deprotection with piperidine, the side-chain to side-chain ($^2\text{Asp-}^7\text{Lys}$) cyclization was carried out using benzotriazol-1-yl-oxy-tris(dimethylamino)-phosphonium hexafluorophosphate (BOP reagent). Cyclization was as described in Di Maio, J., et al., *J. Med. Chem.*, 33:661-667 (1990); and Felix, A.M., et al., *Int. J. Pept. Prot. Res.*, 32:441 (1988). The $^{2,7}\text{cyclo-[}^2\text{Asp,}^7\text{Lys]}$ amylin-MBHA-resin obtained after cyclization was cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{2,7}\text{cyclo-[}^2\text{Asp,}^7\text{Lys]}$ -h-amylin [SEQ ID NO:6]

(SEQ ID NO:6) was purified by preparative HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. FAB mass spec: (M+1)/e=3925.

Please replace the paragraph beginning at page 34, line 17 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of des-¹Lys-h-Amylin [SEQ ID NO:7] (SEQ ID NO:7)

Solid phase synthesis of des-¹Lys-h-amylin (also represented as ²⁻³⁷h-amylin) **[SEQ ID NO:7] (SEQ ID NO:7)** using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-¹Lys-h-amylin **[SEQ ID NO:7] (SEQ ID NO:7)** was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3,775.

Please replace the paragraph beginning at page 35, line 1 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of ¹Ala-h-Amylin [SEQ ID NO:8] (SEQ ID NO:8)

Solid phase synthesis of ¹Ala-h-amylin **[SEQ ID NO:8] (SEQ ID NO:8)** using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin- MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic

acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ¹Ala-h-amylin [SEQ ID NO:8] (SEQ ID NO:8) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3,847.

Please replace the paragraph beginning at page 35, line 14 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of ¹Ser-h-Amylin [SEQ ID NO:9] (SEQ ID NO:9)

Solid phase synthesis of ¹Ser-h-amylin [SEQ ID NO:9] (SEQ ID NO:9) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin- MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ¹Ser-h-amylin [SEQ ID NO:9] (SEQ ID NO:9) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3,863.

Please replace the paragraph beginning at page 35, line 26 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of ²⁹Pro-h-Amylin [SEQ ID NO:10] (SEQ ID NO:10)

Solid phase synthesis of this analogue of human amylin using methylbenzhydrylamine

anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ²⁹Pro-h-amylin **[SEQ ID NO:10] (SEQ ID NO:10)** was purified by preparative HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3916.

Please replace the paragraph beginning at page 36, line 10 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of ^{25,28}Pro-h-Amylin **[SEQ ID NO:11] (SEQ ID NO:11)**

Solid phase synthesis of ^{25,28}Pro-h-amylin **[SEQ ID NO:11] (SEQ ID NO:11)** using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ^{25,28}Pro-h-amylin **[SEQ ID NO:11] (SEQ ID NO:11)** was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3,939.

Please replace the paragraph beginning at page 36, line 23 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of des-¹Lys^{25,28}Pro-h-Amylin [SEQ ID NO:12] (SEQ ID NO:12)

Solid phase synthesis of des-¹Lys^{25,28}Pro-h-amylin [SEQ ID NO:12]
(SEQ ID NO:12) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-¹Lys^{25,28}Pro-h-amylin SEQ ID NO:12 was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3,811.

Please replace the paragraph beginning at page 37, line 8 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of des-¹Lys¹⁸Arg^{25,28}Pro-h-Amylin [SEQ ID NO:13] (SEQ ID NO:13)

Solid phase synthesis of des-¹Lys¹⁸Arg^{25,28}Pro-h-amylin [SEQ ID NO:13]
(SEQ ID NO:13) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-¹Lys¹⁸Arg^{25,28}Pro-h-amylin SEQ ID NO:13 was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid

analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+=3,832$.

Please replace the paragraph beginning at page 37, line 21 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of des-¹Lys¹⁸Arg^{25,28,29}Pro-h-Amylin [SEQ ID NO:14] (SEQ ID NO:14)

Solid phase synthesis of des-¹Lys¹⁸Arg^{25,28,29}Pro-h-amylin [SEQ ID NO:14] (SEQ ID NO:14) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-¹Lys¹⁸Arg^{25,28,29}Pro-h-amylin [SEQ ID NO:14] (SEQ ID NO:14) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+=3,843$.

Please replace the paragraph beginning at page 38, line 6 of the Substitute Specification filed September 29, 2005, with the following amended paragraph:

Preparation of des-¹Lys^{25,28,29}Pro-h-Amylin [SEQ ID NO:15] (SEQ ID NO:15)

Solid phase synthesis of des-¹Lys^{25,28,29}Pro-h-amylin [SEQ ID NO:15] (SEQ ID NO:15) using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with

thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-¹Lys^{25,28,29}Pro-h-amylin **[SEQ ID NO:15] (SEQ ID NO:15)** was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+H)⁺=3,823.

Please delete Example 21 beginning at page 38, line 69 of the Substitute Specification filed September 29, 2005.

Please delete Example 22 beginning at page 39, line 1 of the Substitute Specification filed September 29, 2005.